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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/623,150	07/18/2003	Anne Marie Heegaard	59573(46865)	5193

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EXAMINER

GARVEY, TARA L

ART UNIT PAPER NUMBER

1636

DATE MAILED: 02/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/623,150	HEEGAARD ET AL.	
	Examiner	Art Unit	
	Tara L. Garvey	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 November 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 9-11 and 18-27 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 9-11 and 18-27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 9-11 and 18-27 are pending. Receipt is acknowledged of an amendment filed on November 23, 2005 in which claim 10-11 were amended, claims 12-17 were canceled and new claimed 18-27 are added.

Oath/Declaration

Receipt of a new declaration filed on January 24, 2006 is acknowledged.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Denmark on 23 January 2001. It is noted, however, that applicant has not filed a certified copy of the PA 2001 00118 application as required by 35 U.S.C. 119(b). The office has still not received a certified copy of the Denmark application.

Response to Arguments

Claim Objections

The objection to claims 11-14 is withdrawn in view of applicant's amendment or cancellation of the claims.

Claim Rejections - 35 USC § 102

The rejection of claims 13-15 and 17 under 35 U.S.C. 102(a) is withdrawn in view of applicant's cancellation of the claims.

Claim Rejections - 35 USC § 112

The rejection of claims 9, 10, 13-17 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of applicant's amendment or cancellation of the claims.

The rejection of claims 13-17 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is withdrawn in view of applicant's cancellation of the claims.

The rejection of claims 10 and 12 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of applicant's amendment or cancellation of the claims.

The rejection of claims 13, 14 and 16 under 35 U.S.C. 112, second paragraph and 35 U.S.C. 101 is withdrawn in view of applicant's cancellation of the claims.

New Grounds of Rejection

Claim Objections

Claim 25 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 26 limits claim 25 to "said test cell comprises the chloride channel CIC-7",

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but claim 25 already has the limitation that the "test cell comprises the chloride channel CIC-7."

Claim 18 is objected to because of the following informalities: In line 4, "of the compounds" should be removed. Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 9, 18 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Aromataris et al (British Journal of Pharmacology (1999) volume 126, pages 1375-1382).

Claims 9, 18 and 23 are drawn to a method of screening chemical compounds for activity in treatment, prevention of alleviation of an osteoclast related bone disease in a subject that comprises providing a test cell that comprises one or more chloride channels of the CIC family, subjecting the cell to the compound and measure the ability of the compound to block the chloride channels.

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Aromataris et al teaches expression of the rat CIC-1 channel in Sf-9 cells, exposing the cells to RS-(+) 2-(4-chlorophenoxy)propionic acid and its enantiomer and measuring the activity of the chloride channel using patch-clamp experiments (abstract, page 1376, left column bridging right column and page 1377, Figure 1 and Table 1). Although Aromataris et al does not disclose that the method is to be used for evaluating the activity of the compound in the treatment, prevention or alleviation of an osteoclast related bone disease in a subject as recited in the preamble of the instant claims, a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). In the instant case, there is no difference in the process steps recited in the claims and the process disclosed in Aromataris et al, and there does not appear to be any active process steps implied by the preamble which are not comprised by the method of Aromataris et al. Therefore, absent evidence to the contrary, the process of Aromataris et al is the same as the process claimed.

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Claims 9, 18 and 23 are rejected under 35 U.S.C. 102(a) as being anticipated by Pusch et al (Molecular Pharmacology (2000) volume 58(3), pages 498-507).

Claims 9, 18 and 23 are drawn to a method of screening chemical compounds for activity in treatment, prevention or alleviation of an osteoclast related bone disease in a subject that comprises providing a test cell that comprises one or more chloride channels of the CIC family, subjecting the cell to the compound and measure the ability of the compound to block the chloride channels.

Pusch et al teaches expressing human CIC-1, rat CIC-2, human CIC-5 and the *T. marmorata* channel CIC-0 in *X. laevis* oocytes and determining the effects of enantiomers of 2-(9-chlorophenyl)propionic acid (CPP) and its analogs on the cells by two-microelectrode voltage-clamp measurements and patch clamp measurements for analysis of the channel activity (abstract, page 498, right column, last paragraph to page 500, left column and page 502, right column, third full paragraph through page 503). Although Pusch et al does not disclose that the method is to be used for evaluating the activity of the compound in the treatment, prevention or alleviation of an osteoclast related bone disease in a subject as recited in the preamble of the instant claims, a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190

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USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). In the instant case, there is no difference in the process steps recited in the claims and the process disclosed in Pusch et al, and there does not appear to be any active process steps implied by the preamble which are not comprised by the method of Pusch et al. Therefore, absent evidence to the contrary, the process of Pusch et al is the same as the process claimed.

Claim Rejections - 35 USC § 112

Claim 9-11 and 18-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art, relative skill in the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claim, with the most relevant discussed below.

Nature of the invention: The claims are drawn to method of screening chemical compounds for activity in treatment, prevention of alleviation of an osteoclast related bone disease in a subject that comprises providing a test cell that comprises one or more chloride channels of the CIC family, subjecting the

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cell to the compound and measure the ability of the compound to block the selected chloride channels.

Breadth of the claim: The claims are broad in that they encompass screening various chemical compounds for their ability to treat any osteoclast disorder by determining the ability of the compound to modulate any CIC chloride channel in any test cell.

Guidance in the specification/Existence of a working example: The specification has not demonstrated that any of the CIC family members are involved in osteoclast disorders. The specification provides working examples that demonstrate the expression by northern blot analysis of CIC-7 in human osteoclasts and upregulation during osteoclast differentiation, but the expression of the other two tested CIC channels, CIC-3 and CIC-6, was not detected (page 14-15). The applicant's conclude that "CIC-3 and CIC-6 are not significantly expressed in osteoclasts" since they are only detected in the more sensitive RT-PCR analysis (page 15).

Furthermore, the specification provides HEK293, which are human embryonic kidney cells, recombinantly expressing CIC-3, CIC-6 and CIC-7 for screening compounds that have the ability to block the chloride channels by patch clamp analysis. The specification has not provided methods on how to select for compounds that block CIC-7 and not CIC-1, CIC-2, CIC-4, CIC-5, CIC-Ka and CIC-Kb in any test cell. In addition, the specification has not demonstrated that identification of any compound that can block any CIC family member or specifically CIC-7 will result in a potential compound that can treat,

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prevent or alleviate an osteoclast disorder. In particular, a correlation between the level of inhibition of any chloride channel by a compound and the ability of that compound to be useful as a therapeutic has not been demonstrated.

State of the art/Predictability of the art: At the effective time of filing and presently, the only CIC family member known to be involved in an osteoclast disorder is CIC-7. Specifically, briefly prior to the effective filing date of the instant application, Kornack et al demonstrated a correlation between loss of the CIC-7 chloride channel and osteopetrosis (Kornack et al. Cell (2001) volume 104, pages 205-215 as cited in the IDS submitted on February 13, 2004), but no relation between CIC-7 and osteopetrosis, Paget's disease of bone or osteolytic cancer invasion had been identified. The other family members have not been shown to be involved in osteoclast disorders. Rather, the other members have been shown to be involved in renal, muscular and neurological disorders. For instance, CIC-3 has been shown to be involved in CNS degeneration in a mouse model, CIC-1 is involved in human myotonia, CIC-5 is involved in kidney disorder such as Dent's disease and the role of CIC-6 in human disease remains unknown (George et al. Current biology (2001) volume 11, pages R620-R628; see page R621, Table 1; Jentsch et al. Current Opinion in Neurobiology (2005) volume 15, pages 319-325; see page 321, Table 1).

Quantity of experimentation: A large amount of experimentation would be necessary to determine if the chemical compounds found to block CIC chloride channels in any test cell would provide potential compounds for the treatment of

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any osteoclast disorders since the specification nor the art has demonstrated that all the CIC family channel members are involved in all osteoclast disorders.

Conclusion: In order to practice the claimed invention, the skilled artisan would not have found sufficient guidance in the specification to screen chemical compounds as potential therapeutic agents for osteoclast related disorders for their ability to block CIC chloride channels. The prior art did not compensate for the lack of guidance in the specification since the teachings do not recognize a role for CIC chloride channels other than CIC-7 in the normal or diseased osteoclast. The skilled artisan would have had to engage in a large amount of experimentation to practice the claimed invention. In view of the lack of guidance and the large amount of experimentation in an unpredictable art, it would require undue experimentation to practice the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 9 recites the limitation "the channel compound" in line 6. There is insufficient antecedent basis for this limitation in the claim.

Double Patenting

Applicant is advised that should claims 9-11 be found allowable, claims 18, 23, 24 and 27 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight

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difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tara L Garvey whose telephone number is (571) 272-2917. The examiner can normally be reached on Monday through Friday 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Tara L Garvey
Examiner
Art Unit 1636

TLG



JAMES KETTER
PRIMARY EXAMINER